IN THE CLAIMS

1-64. (Cancelled).

65. (New) A method of analysing fluorescence emitted by radiation excited samples in an array of samples when used to perform immediate fluorescence analysis or time resolved fluorescence analysis, comprising the steps of focusing light emitted from each said sample at infinity so as to form a parallel beam, in parallel with the light from all of the other sample sites making up the array, subsequently focusing all the parallel light paths through a single point and locating at the point a small aperture to restrict unwanted light from fluorescing material upstream and downstream of the sites of interest in the samples, and re-establishing a parallel array of light beams by the use of a further lens so as to present to an addressable detector array a plurality of parallel light paths corresponding to the light paths from the samples, and individually addressing different regions of the detector array onto which the parallel light paths impinge, to determine the light incident thereon, and storing data relating to the quantity of incident light on each said region of the detector array together with address information to enable the data to be reconciled with the position of the sample in the array on the substrate to which that data relates, in which a shutter is provided to inhibit the transfer of light to the detector, excitation radiation is supplied for a short interval of time and then shut off (either by pulsing the source out using further shutter or both), after a selected interval of time the shutter preventing transfer of light to the detector is opened and after an appropriate integration interval, the residual charge pattern on the charge coupled detector array is interrogated to generate a signal relating to the charge pattern (and therefore indicative of light incident thereon) for processing and storage as aforesaid.

66. (New) The method according to claim 65, further comprising the step of introducing periodically into the optical system excitation wavelength illumination and projecting same through the optical imaging devices associated with the array of samples to project the excitation illumination onto a specific region in each said sample, thereafter extinguishing the excitation wavelength light and enabling fluorescence caused by the excitation to pass through the same optical devices to emerge as parallel rays of light for transfer to the detector.

67. (New) The method according to claim 65, wherein objective lenses are arranged above or below the sample array.

68. (New) A method of imaging a plurality of micro-sample light emitting sites simultaneously onto separately addressable detectors so that light emitted from each site is

monitorable by one of the detectors, wherein a corresponding plurality of objective lenses are located adjacent to the micro-sample array with one objective lens for each micro-sample, the latter are located at or near the focal point of each of the lenses so that light emanating from each micro-sample is collected by its respective objective lens and converted into a beam of parallel or near parallel rays, the objective lenses are arranged so that the axes of all the beams issuing therefrom are parallel and spaced apart, and the beams are focused by a focusing lens through a single point and collected beyond that point by detector lens means which serves to reconstitute the parallel beams for presentation to the detector array, in which a small aperture pinhole is placed at the focal point of the focusing lens so that light which is not emanating from the focal point of each of the objective lenses adjacent the micro-sample sites will be out of focus at the small aperture pinhole, wherein a filter is located in front of the detector, and apertured masks are placed on either side of the filter to collimate the parallel beam to further reduce background and cross-talk.

69. (New) A method according to claim 68, wherein the axes of the objective lenses are angled with appropriate adjustment of the optical characteristics of the objective and/or the other lenses.

70. (New) A method according to claim 68, wherein the focusing lens is a multi-component lens employed for directing all the beam paths through the single point.

71. (New) A method according to claim 68, wherein the micro-samples are positioned relative to the micro-sample objective lenses so that the region of interest is as close as possible to the focal point of the respective objective lens.

72. (New) A method according to claim 68, wherein the samples are located on a planar support with the regions of interest all in the same plane so that the objective lenses are likewise all locatable in the same plane parallel to that containing the regions of interest in the samples.

73. (New) A method according to claim 68, including the step of adjusting the position of the micro-sample array relative to the lens array and also the step of individually adjusting the position of at least the objective lenses relative to the micro-samples or vice versa to ensure that the regions of interest in the micro-samples are at the focal point of the respective micro-sample objective lenses.

74. (New) A method according to claim 68, wherein in order to provide spectral separation based on wavelength, a filter is included in the light path either between the micro-sample objective lenses and the focusing lens means ahead of the pinhole, or between the detector lens and the detector array.

75. (New) A method according to claim 74, wherein the spectral filter is located in a region in which the light paths are parallel or nearly parallel.

76. (New) A method according to claim 68, according to which where fluorescence is the mechanism which generates the radiation which is to be focused onto a detector, excitation radiation to produce the fluorescence is applied only to a region of interest within each micro-sample rather than over the whole of the micro-sample.

77. (New) A method according to claim 76, wherein excitation radiation is injected into the multipath optical system so as to proceed in a parallel sense towards the array of objective lenses, in an opposite sense to the light which emanates from the micro-samples, so as to be focused by the objective lenses onto the region of interest in each micro-sample.

78. (New) A method according to claim 77, wherein the excitation radiation is injected as a parallel beam into the optical path, at right angles thereto, and a 45° beam splitting device is provided onto which the parallel excitation radiation is incident and from which it is directed in a parallel manner towards the objective lenses, but through which radiation from the micro-samples can pass to the focusing lens.

79. (New) A method according to claim 68, wherein excitation radiation is produced using a laser such as an argon ion laser, and a beam expander is employed to expand the cross-section of the laser beam into a relatively large area beam equivalent to the area of the parallel array of objective lenses.

80. (New) A method according to claim 68, having an 8 x 12 array of objective lenses on the same 8 x 12 matrix as a standard 96 well plate, and a well plate is moved using an XY stage relative to the array of objective lenses so as to present groups of 96 wells to the 96 lens array.

81. (New) A method according to claim 68, wherein the parallel beams of light directed towards the detector array are transferred to the said array via optical fibres, in the form of a fibre optic bundle or fibre optic plate.

82. (New) A method according to claim 81, wherein where a bundle of fibres is employed, the arrangement of the fibres in the bundle differs between the input and output ends thereof so that the array of fibres which convey the light paths to the different regions of the detector array conforms more to the shape of the detector array in the XY plane.

83. (New) A method according to claim 68, wherein the detector array is a charge coupled device having a large number of separately addressable regions (each of which is commonly referred to as a pixel) and groups of adjacent pixels (or individual pixels) from the detector for each sample are addressed, to enable good resolution to be obtained in the XY sense in relation to the light from one sample and another.

84. (New) A method according to claim 83, wherein the charge coupled device is cooled, for example cryogenically.

85. (New) A method according to claim 68 wherein the detector array comprises an array of photomultipliers, one photomultiplier for each of the channels (optical paths).

86. (New) A method according to claim 85, wherein each photomultiplier has a window, and optical fibres or bundles forming cables are employed to convey the light from each of the apertures in a mask to the windows of photo-multipliers which together occupy an area considerably greater than that of the mask.

87. (New) A method according to claim 85, wherein the photomultipliers are gated electronically so as to enable the delays and short integration periods to be generated as required by time resolved fluorescence or luminescence applications.

88. (New) A method according to claim 68, wherein the detector array comprises an image intensifier or an intensified CCD.

89. (New) A method according to claim 88 wherein the image intensifier or intensified CCD is gated electronically so as to enable the delays and short integration periods to be generated as required by time resolved fluorescence or luminescence applications.

90. (New) A method according to claim 68, wherein further lenses for focusing the parallel beams of light directed towards the detector array are employed to improve resolution at the detector surface either in combination with a fibre optic transfer bundle.

91. (New) A method according to claim 68, wherein micro lenses, optionally in combination with a fibre optic transfer plate, are employed in the objective lenses adjacent the micro-samples.

92. (New) A method according to claim 91, in which micro lenses have one infinite conjugate.

93. (New) Apparatus adapted for performing the method of claim 68, wherein a filter is located in front of the detector, and apertured masks are placed on either side of the filter to collimate the parallel beam to further reduce background and cross-talk, comprising means for supporting a micro-sample array on a substrate in close proximity but parallel to an array of objective lenses arranged so as to correspond on a one to one basis with the positions and spacing of at least some of the micro-samples on the substrate, each of the objective lenses having a focal length and being positioned relative to a region of its related micro-sample by a distance equal to the focal length of the lens so that light emitted from that region of the micro-sample will emerge from the lens as a parallel beam parallel to the axis of the lens, and the parallel beams of light are focused by means of a single focusing lens onto a detector lens so as to produce an image of the micro-sample light emissions in a plane of an array of individually addressable photoelectric detectors, such as regions of an addressable CCD array, including a pinhole aperture at the focal point of the focusing lens so as to improve the on-axis resolution of the optical system and assist in attenuating unwanted fluorescence such as from background material and other components of an assay ahead of or behind the region of interest in a micro-sample measured along the optical axis of the objective, from reaching the detectors, including shutter means to inhibit the passage of the source light, except when required for excitation purposes, and further shutter means synchronised with that associated with the source to prevent light of any wavelength reaching the detector whilst excitation light is projected into the system and circuit means is provided to which signals read out from

the array are supplied, each signal corresponding to the light incident on a region of the detector for a given period of time from one of the micro-samples, and computing and analysing circuit means is provided, responsive to the electrical signals, together with memory means for storing data indicative of the light found to be emitted from each of the micro-samples, for storing those values together with address information, whereby each stored value is identifiable with the micro-sample on the substrate from which the light giving that value has been emitted by reference to the position of the region in the detector array and by correlating the position of the sample in the sample array.

94. (New) Apparatus according to claim 93, further including a beam splitter, such as a dichroic mirror, interposed in the optical path between the objective lenses and the focusing lens to enable on the one hand light to pass from the lenses to the focusing lens, and on the other hand to enable excitation radiation, typically light of a particular wavelength, to be reflected as a parallel beam towards the objective lenses, thereby utilising the optical focusing characteristics of the objective lenses to focus the parallel light into spots of light which register with the micro-samples so that the latter are individually radiated by excitation light which is predominantly incident on that region of each micro-sample which is to be inspected for fluorescence after the excitation radiation has been removed, and filter means provided in the optical path between the beam splitter and the detector array to generally attenuate any excitation wavelength radiation travelling towards the detector and generally prevent such radiation from reaching the detector.

95. (New) Apparatus according to claim 93, including a laser source as the source of excitation radiation, and a beam expander for enlarging the cross-section of the laser beam and presenting a generally uniform parallel beam of excitation radiation for entry into the imaging system via the beam splitter or dichroic mirror.

96. (New) A method of imaging a plurality of micro-sample light emitting sites simultaneously onto separately addressable detectors so that light emitted from each site is monitorable by one of the detectors, wherein a corresponding plurality of objective lenses are located adjacent to the micro-sample array with one objective lens for each micro-sample, the latter are located at or near the focal point of each of the lenses so that light emanating from each micro-sample is collected by its respective objective lens and converted into a beam of parallel or near parallel rays, the objective lenses are arranged so that the axes of all the beams issuing therefrom are parallel and spaced apart, and the beams are focused by a

focusing lens through a single point and collected beyond that point by detector lens means which serves to reconstitute the parallel beams for presentation to the detector array, wherein a single small aperture pinhole is placed at the focal point of the focusing lens so that light which is not emanating from the focal point of each of the objective lenses adjacent the micro-sample sites will be out of focus at the small aperture pinhole, and in that there is further provided an array of 96 micro-lenses positioned so as to image each region down on a spot of small size at the surface of the detector.

97. (New) Apparatus adapted for performing the method of claim 96 in which there is provided an array of 96 micro-lenses positioned so as to image each region down on a spot of small size at the surface of the detector, comprising means for supporting a micro-sample array on a substrate in close proximity but parallel to an array of objective lenses arranged so as to correspond on a one to one basis with the positions and spacing of at least some of the micro-samples on the substrate, each of the objective lenses having a focal length and being positioned relative to a region of its related micro-sample by a distance equal to the focal length of the lens so that light emitted from that region of the micro-sample will emerge from the lens as a parallel beam parallel to the axis of the lens, and the parallel beams of light are focused by means of a single focusing lens onto a detector lens so as to produce an image of the micro-sample light emissions in the plane of an array of individually addressable photoelectric detectors, such as regions of an addressable CCD array, including a single small aperture pinhole at the focal point of the focusing lens so as to improve the on-axis resolution of the optical system, and to assist in attenuating unwanted fluorescence such as from background material and other components of an assay ahead of or behind the region of interest in a micro-sample measured along the optical axis of the objective from reaching the detectors, including shutter means to inhibit the passage of the source light, except when required for excitation purposes, and further shutter means synchronised with that associated with the source to prevent light of any wavelength reaching the detector whilst excitation light is projected into the system and circuit means is provided to which signals read out from the array are supplied, each signal corresponding to the light incident on a region of the detector for a given period of time from one of the micro-samples, and computing and analysing circuit means is provided, responsive to the electrical signals, together with memory means for storing data indicative of the light found to be emitted from each of the micro-samples, for storing those values together with address information, whereby each stored value is identifiable with the micro-sample on the substrate from which the light giving

that value has been emitted by reference to the position of the region in the detector array and by correlating the position of the sample in the sample array.

98. (New) Apparatus according to claim 97, further including a beam splitter, such as a dichroic mirror, interposed in the optical path between the objective lenses and the focusing lens to enable on the one hand light to pass from the lenses to the focusing lens, and on the other hand to enable excitation radiation, typically light of a particular wavelength, to be reflected as a parallel beam towards the objective lenses, thereby utilising the optical focusing characteristics of the objective lenses to focus the parallel light into spots of light which register with the micro-samples so that the latter are individually radiated by excitation light which is predominantly incident on that region of each micro-sample which is to be inspected for fluorescence after the excitation radiation has been removed, and filter means provided in the optical path between the beam splitter and the detector array to generally attenuate any excitation wavelength radiation travelling towards the detector and generally prevent such radiation from reaching the detector.

99. (New) Apparatus according to claim 97, including a laser source as the source of excitation radiation, and a beam expander for enlarging the cross-section of the laser beam and presenting a generally uniform parallel beam of excitation radiation for entry into the imaging system via the beam splitter or dichroic mirror.

100. (New) A method of imaging a plurality of micro-sample light emitting sites simultaneously onto separately addressable detectors so that light emitted from each site is monitorable by one of the detectors, wherein a corresponding plurality of objective lenses are located adjacent to the micro-sample array with one objective lens for each micro-sample, the latter are located at or near the focal point of each of the lenses so that light emanating from each micro-sample is collected by its respective objective lens and converted into a beam of parallel or near parallel rays, the objective lenses are arranged so that the axes of all the beams issuing therefrom are parallel and spaced apart, and the beams are focused by a focusing lens through a single point and collected beyond that point by detector lens means which serves to reconstitute the parallel beams for presentation to the detector array, in which a small aperture pinhole is placed at the focal point of the focusing lens so that light which is not emanating from the focal point of each of the objective lenses adjacent the micro-sample sites will be out of focus at the small aperture pinhole, wherein the detector array comprises an array of photomultipliers, one photomultiplier for each of the optical paths.

101. (New) Apparatus adapted for performing the method of claim 100 wherein the detector array comprises an array of photomultipliers, one photomultiplier for each of the optical paths, comprising means for supporting a micro-sample array on a substrate in close proximity but parallel to an array of objective lenses arranged so as to correspond on a one to one basis with the positions and spacing of at least some of the micro-samples on the substrate, each of the objective lenses having a focal length and being positioned relative to a region of its related micro-sample by a distance equal to the focal length of the lens so that light emitted from that region of the micro-sample will emerge from the lens as a parallel beam parallel to the axis of the lens, and the parallel beams of light are focused by means of a single focusing lens onto a detector lens so as to produce an image of the micro-sample light emissions in the plane of an array of individually addressable photoelectric detectors, such as regions of an addressable CCD array, including a pinhole aperture at the focal point of the focusing lens so as to improve the on-axis resolution of the optical system and assist in attenuating unwanted fluorescence such as from background material and other components of an assay ahead of or behind the region of interest in a micro-sample measured along the optical axis of the objective, from reaching the detectors, including shutter means to inhibit the passage of the source light, except when required for excitation purposes, and further shutter means synchronised with that associated with the source to prevent light of any wavelength reaching the detector whilst excitation light is projected into the system and circuit means is provided to which signals read out from the array are supplied in the form of a sequence of digital values or otherwise, each corresponding to the light incident on a region of the detector for a given period of time from one of the micro-samples, and computing and analysing circuit means is provided, responsive to the electrical signals, together with memory means for storing data indicative of the light found to be emitted from each of the micro-samples, for storing those values together with address information, whereby each stored value can be identified with the micro-sample on the substrate from which the light giving that value has been emitted by reference to the position of the region in the detector array and by correlating the position of the sample in the sample array.

102. (New) Apparatus according to claim 101, further including a beam splitter, such as a dichroic mirror, interposed in the optical path between the objective lenses and the focusing lens to enable on the one hand light to pass from the lenses to the focusing lens, and on the other hand to enable excitation radiation, typically light of a particular wavelength, to be reflected as a parallel beam towards the objective lenses, thereby utilising the optical focusing

characteristics of the objective lenses to focus the parallel light into spots of light which register with the micro-samples so that the latter are individually radiated by excitation light which is predominantly incident on that region of each micro-sample which is to be inspected for fluorescence after the excitation radiation has been removed, and filter means provided in the optical path between the beam splitter and the detector array to generally attenuate any excitation wavelength radiation travelling towards the detector and generally prevent such radiation from reaching the detector.

103. (New) Apparatus according to claim 101, including a laser source as the source of excitation radiation, and a beam expander for enlarging the cross-section of the laser beam and presenting a generally uniform parallel beam of excitation radiation for entry into the imaging system via the beam splitter or dichroic mirror.

104. (New) A method of measurement of radiation from a plurality of sample sites, wherein a plurality (N) of single channel confocal optical systems and photoelectric detectors or detecting areas are arranged in parallel to form a plurality of reading heads arranged side-by-side so as simultaneously to read a corresponding plurality of adjacent sample sites emitting radiation, wherein the reading heads are independently adjustable so that each is accurately positionable over or under a sample site.

105. (New) A method according to claim 103, wherein the sites are arranged in a column or in an array, and the optical systems are arranged in a single line for reading column by column of a multi-column array, or in a staggered pattern for simultaneously viewing sites in different columns.

106. (New) A method according to claim 103, using (N) independent confocal systems, each with its optic axis aligned with one sample site.

107. (New) A method according to claim 103, wherein light from a single laser source is split into an appropriate plurality of beams, conveyed each by a fibre optic cable to individual sample sites.

108. (New) A method according to claim 103, wherein light emitted from the separate sites is conveyed to individual detectors, or discrete regions of an array detector, via optical fibres.

109. (New) A method according to claim 103, wherein a special opto-mechanical device is provided to bring each scanner's optic axis into alignment by means of an appropriate scan in the Y-direction.

REMARKS

The examiner's reconsideration of the application is requested in view of the new claim set above and comments which follow.

In the office action, the examiner has rejected the now-cancelled claims 33-64 under 35 U.S.C. §112 as being indefinite. The new claim set has been cast, taking into consideration the matters raised by the examiner. It is believed that the new claims meet all requirements of 35 U.S. C. §112.

There are now five independent claims in the present application, and they correspond to the underlying international application as follows:

Independent Claim	Basis in PCT application
65	Claim 1 + claim 6
68	Claim 1 + claim 33, and p. 14, line 9
96	Claim 1 + last paragraph of p. 20
99	Claim 1 + claim 26
104	Claim 1 + claim 38

The claims of the corresponding UK application were rejected on the same prior art as that cited in the present application, and the new claims above were substituted and later granted.

The examiner has rejected former claims 33-64 under 35 U.S.C. §103 on the basis of obviousness, as set forth in the rejection beginning on the bottom of page 3 of the office action. With the cancellation of the rejected claims and substitution of the new claim set, it is believed that the rejection is now moot. The method claims properly define the method, having steps not found in the references, and the apparatus claims similarly defined the apparatus over the prior art.

It is therefore submitted that this application distinguishes from the known prior art and is allowable thereover. The examiner's further and favorable reconsideration is therefore urged.

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